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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BLANCHARD, DAVID J	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/905,083	O'BRIEN, TIMOTHY I.	
	Examiner	Art Unit	
	David J Blanchard	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *1/9/2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *26-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *26-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 22-25 have been cancelled in the Paper filed 1/9/2004.

2. This office action sets forth New Grounds of Rejections.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

4. Claims 26-31 are pending and under examination.

Specification

5. The disclosure is objected to because of the following informalities:

a. The priority statement on the first line of the specification should be updated to indicate that the instant application is a DIV of 09/502,600 filed 02/11/2000, now U.S. Patent 6,294,344 and is a CIP of 09/039,211 filed 03/14/1998, now U.S. Patent 6,303,318.

b. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

Appropriate correction is required.

Claim Objections

6. Claim 27 is objected to because of the following informalities:

Claim 27 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 27 recites that the "immune-activated cells are selected from the group consisting of B cells, T cells and dendrites", which does not further limit or narrow the scope of parent claim 26 from which claim 27 depends. Claim 26 is limited to a method of producing activated dendritic cells or immune-activated cells.

Rejections Withdrawn

7. The rejection of claims 22-25 under 35 U.S.C. 112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn because claims 22-25 have been cancelled in the Paper filed 1/9/2004.

New Grounds of Rejections

8. Claims 26-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 26-31 are indefinite for reciting "producing immune-activated cells" and "exposing dendritic cells" in claim 26. Is the method of "producing immune-activated cells" drawn to producing activated dendritic cells or is the method drawn to producing other immune-activated cells such as B cells and T cells by first exposing dendritic cells to a stratum corneum chymotrytic enzyme or are the B cells and T cells activated by direct exposure to a stratum corneum chymotrytic enzyme?

b. Claim 27 is indefinite for reciting "dendrites." Dendrites are part of a neuron and are not immune cells (i.e., dendritic cells). Did applicant intend to recite "dendritic cells" as the immune-activated cells? Applicant is advised that a recitation of "dendritic cells" in dependent claim 27 would not further limit the parent claim, claim 26, because claim 26 already recites "dendritic cells" in the method of producing immune-activated cells (see item 6 above).

9. Claims 26-31 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was fled, had possession of the claimed invention.

The specification does not reasonably provide a written description for (1) a method of producing immune-activated cells directed toward any "stratum corneum chymotrytic enzyme" comprising the steps of exposing dendritic cells to any "stratum corneum chymotrytic enzyme" or any fragments thereof that lack "stratum corneum chymotrytic enzyme" protease activity wherein said exposure to said "stratum corneum chymotrytic enzyme" or fragment thereof activates said dendritic cells thereby producing immune-activated cells directed toward any "stratum corneum chymotrytic enzyme", (2) the said method wherein said immune cells are B cells, T cells, and dendrites, (3) the said method wherein the dendritic cells are isolated from an individual prior to exposure to any "stratum corneum chymotrytic enzyme" or any fragment thereof wherein said dendritic cells are reintroduced into said individual subsequent to said exposure, (4) the said method wherein said individual with any cancer, or suspected of having any cancer or at risk of getting any cancer, and (5) the said method wherein any "stratum corneum chymotrytic enzyme" fragment "is" from 9 amino acids to 20 amino acids.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form selected 9-mer peptides of the human "stratum corneum chymotrytic enzyme" (i.e., SEQ ID NOS. 31, 32, 33, 34, 35, 36, 80, 86 and 99).

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

The specification discloses only the cDNA encoding the human "stratum corneum chymotrytic enzyme" of SEQ ID NO:30, and encoded 9-mer peptides thereof of SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99. The specification does not disclose the full-length human "stratum corneum chymotrytic enzyme" polypeptide and does not disclose any "stratum corneum chymotrytic enzyme" fragment other than the human 9-mer "stratum corneum chymotrytic enzyme" peptides of SEQ ID NOS. 31-136. The "stratum corneum chymotrytic enzyme" is shown to be frequently expressed in ovarian tumors (See Example 13, Tables 5 and 7) as detected by immunohistochemical staining and Northern blot analysis. Based on the level of "stratum corneum chymotrytic enzyme" expression in ovarian tumor cells, applicant asserts that the "stratum corneum chymotrytic enzyme" or fragment thereof is useful for adaptive immunotherapy by exposing immune cells such as dendritic, T or B cells to any "stratum corneum chymotrytic enzyme" or any peptide fragment thereof and reintroducing said "immune-activated cells into the patient from whom the cells were isolated would be useful for treating just any cancer.

Further, the term "is" in claim 26 is interpreted as "comprising", meaning that the "stratum corneum chymotrytic enzyme" fragments from 9 amino acids to 20 amino acid acids can have additional amino acid residues at either the N- or C-terminus or both termini. There is inadequate written description about the innumerable undisclosed

amino acids to be added and whether the "stratum corneum chymotrytic enzyme" fragment containing said additional amino acid residues has the same function as the full-length human "stratum corneum chymotrytic enzyme" that lacks "stratum corneum chymotrytic enzyme" protease activity. Given the lack of written description for the innumerable additional species of "stratum corneum chymotrytic enzyme" including any fragments thereof or fragments having extra amino acids in addition to the fragment that "is" 9 to 20 amino acids in length, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. There is not even an identification of any particular portion of the "stratum corneum chymotrytic enzyme" structure that must be conserved. Thus, Applicant was not in possession of the broadly claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of "stratum corneum chymotrytic enzyme" polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a

potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Other than the specific human "stratum corneum chymotrytic enzyme" encoded by SEQ ID NO:30 and the specific 9-mer "stratum corneum chymotrytic enzyme" fragments of SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99, there is inadequate written description with respect to the structure-function correlation of any "stratum corneum chymotrytic enzyme ", any "fragment thereof that lacks stratum corneum chymotrytic enzyme protease activity", and any stratum corneum chymotrytic enzyme fragment from 9 amino acids to 20 amino acids.

See University of Calfornia v. Eli Lilly and Co. 43 USPQZd 1398. Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 200 1.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

10. Claims 26-31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a method of producing activated immune cells to the human stratum corneum chymotrytic enzyme encoded by SEQ ID NO:30 and 9-mer peptides of SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99, (2) the said method wherein said immune cells are selected from B cells, T cells, and dendritic cells, (3) the said method wherein the dendritic cells are isolated from an individual prior to exposure to the human stratum corneum chymotrytic enzyme or 9-mer peptides of SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99, wherein said dendritic cells are reintroduced into said individual subsequent to said exposure, does not reasonably provide enablement for (1) a method of producing activated immune cells to just any stratum corneum chymotrytic enzyme or just any fragment thereof comprising the steps of exposing dendritic cells to any stratum corneum chymotrytic enzyme or any fragment thereof that lacks stratum corneum chymotrytic enzyme protease activity wherein said exposure to said stratum corneum chymotrytic enzyme or fragment thereof activates immune cells thereby producing activated immune cells directed toward any stratum corneum chymotrytic enzyme, (2) the said method wherein said immune cells are selected from B cells, T cells, and dendritic cells, (3) the said method wherein the dendritic cells are isolated from an individual prior to exposure to any stratum corneum

chymotrytic enzyme or any fragment thereof wherein said dendritic cells are reintroduced into said individual subsequent to said exposure, (4) the said method wherein said individual with any cancer, or suspected of having any cancer or at risk of getting any cancer, and (5) the said method wherein any stratum corneum chymotrytic enzyme fragment is from 9 amino acids to 20 amino acids for adaptive immunotherapy against any cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized In re Wands (858 F2d 731, 737, 8 USPQZd 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only the cDNA (SEQ ID NO:30) encoding the human "stratum corneum chymotrytic enzyme", and 9-mer peptides thereof of SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99. The specification does not disclose the full-length human "stratum corneum chymotrytic enzyme" polypeptide and does not disclose any "stratum corneum chymotrytic enzyme" fragment other than the human 9-mer "stratum corneum chymotrytic enzyme" peptides of SEQ ID NOS. 31-136. The stratum corneum

chymotrytic enzyme is frequently expressed in ovarian tumors (See Example 13, Tables 5 and 7) as detected by immunohistochemical staining and Northern blot analysis. Based on the levels of stratum corneum chymotrytic enzyme expression in ovarian tumor cells, applicant asserts that the human stratum corneum chymotrytic enzyme or any fragment thereof is useful for adaptive immunotherapy by producing immune-activated cells directed toward any stratum corneum chymotrytic enzyme by exposing immune cells such as dendritic, T or B cells with any stratum corneum chymotrytic enzyme or any peptide fragment thereof and reintroducing said immune-activated cells into the patient from whom the cells were isolated would be useful for treating just any cancer.

The declaration of Timothy J. O'Brien filed 2/19/2003 submits that human stratum corneum chymotrytic enzyme 9-mer peptides corresponding to amino acid residues 5-13 and 123-131 of the human stratum corneum chymotrytic enzyme possess binding motifs of HLA class I molecules and were effective at inducing specific CD8+ CTL responses in vitro.

The specification and the declaration do not provide the skilled artisan with sufficient guidance or direction for producing immune-activated cells by exposing dendritic cells to just any "stratum corneum chymotrytic enzyme" or just any fragment thereof wherein the immune-activated cells can be used as adaptive immunotherapy against any cancer commensurate in scope with the claimed invention.

The state of the prior art is such that it is well known that epitopes from a polypeptide must interact with T-cell receptors or be presented on the surface of

antigen-presenting cells in association with MHC molecules in order to stimulate T-cells. While it is known that size is a factor in processing and recognition of an epitope, it is also known that other factors are involved in T cell stimulation, all of which have not been elucidated. For support, see Bixler et al (U.S. patent 5,785,973, column 5, line 47 to column 7, line 59). The prior art of Geysen (U.S. Patent 5,539,084) shows that even for peptides of similar size derived from the same "parent" polypeptide, not all will be capable of interacting with T-cells (column 2, lines 5-9 and Figure 6), thus demonstrating the degree of uncertainty in the art for predicting which subsets or portions of a larger polypeptide will be capable of interacting with or stimulating T-cells. Neither the specification nor the prior art teach specific T cell epitopes of the stratum corneum chymotrytic enzyme, which are known to be capable of stimulating T-cells. Further, the term "is" in claim 28 is interpreted as "comprising", meaning that the stratum corneum chymotrytic enzyme fragment from 9 amino acids to 20 amino acid acids contains additional amino acid residues at either the N- or C-terminus or both termini. There is insufficient guidance as to which amino acids are to be added and whether the stratum corneum chymotrytic enzyme fragment containing the additional amino acids would have the same function as the full-length human stratum corneum chymotrytic enzyme.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications of other types and the positions within the protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining similar biological activity are

limited in any protein. The result of such modifications is unpredictable based on the instant disclosure. One skilled in the art would expect any tolerance to modification shown for a given protein to diminish with each further and additional modification, e.g., multiple substitutions. The sequence of some proteins is highly conserved and one skilled in the art would not expect tolerance to any amino acids modifications in such proteins.

The specification does not support the broad scope of the claims, which encompass all modifications and fragments of the human stratum corneum chymotrytic enzyme because the specification does not disclose the following:

a. The amino acid sequence for the human stratum corneum chymotrytic enzyme;

b. The general tolerance to modification and extent of such tolerance;

c. The specific positions and regions of the sequences which can be predictably modified and which regions are critical;

d. What fragments, if any, can be made which retain the biological activity of the intact protein; and

e. the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Protein chemistry is probably one of the most unpredictable areas of biotechnology. For example, the replacement of a single lysine at position 118 of the acidic fibroblast growth factor by a glutamic acid led to a substantial loss of heparin

binding, receptor binding, and biological activity of the protein (see Burgess et al, Journal of Cell Biology Vol 111 November 1990 2129-2138). In transforming growth factor alpha, replacement of aspartic acid at position 47 with asparagine, did not affect biological activity while the replacement with serine or glutamic acid sharply reduced the biological activity of the mitogen (see Lazar et al Molecular and Cellular Biology Mar 1988 Vol 8 No 3 1247-1252).

Replacement of the histidine at position 10 of the B-chain of human insulin with aspartic acid converts the molecule into a superagonist with 5 times the activity of nature human insulin. Schwartz et al, Proc Natl Acad Sci USA Vol 84:6408-6411 (1987). Removal of the amino terminal histidine of glucagon substantially decreases the ability of the molecule to bind to its receptor and activate adenylate cyclase. Lin et al Biochemistry USA Vol 14:1559-1563 (1975)

For example, Lederman et al (Molecular Immunology 28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document).

For example, Li et al (Proc. Natl. Acad. Sci. USA 77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other activities when constructing analogs (see entire document).

Given the number of undisclosed stratum corneum chymotrytic enzymes and fragments thereof, it is unpredictable which undisclosed stratum corneum chymotrytic enzyme and fragments thereof are useful for a method of producing activated immune cells such as B cells, T cells, and dendritic cells in vitro, let alone reintroduced into any

individual having any cancer or suspected of having any cancer or at risk of getting any cancer as adaptive immunotherapy. With the exception of the full-length human stratum corneum chymotrytic enzyme polypeptide encoded by SEQ ID NO:30 and the specific 9-mer peptides of SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99, applicant has provided insufficient evidence or nexus between any stratum corneum chymotrytic enzyme, any fragment thereof, any stratum corneum chymotrytic enzyme fragment that "is" from 9 amino acids to 20 amino acids, that lack stratum corneum chymotrytic enzyme protease activity for a method of producing activated-immune cells directed toward any stratum corneum chymotrytic enzyme by exposing dendritic cells, B cells or T cells to any stratum corneum chymotrytic enzyme or fragment thereof and reintroducing the activated-immune cells into an individual with any cancer, suspected of having any cancer or at risk of getting any cancer for adaptive immunotherapy.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQZd 1334 (PTO Bd. Pat App. & Inter. 1992). In re wands, 858 F.2d at 737, 8 USPQZd at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary.

In view of the quantity of experimentation necessary, the limited working examples in the specification, the unpredictability of the art as evidenced by Bixler et al, Geysen, Burgess et al, Lazar et al, Schwartz et al, Lin et al, Lederman et al, Li et al and the lack of sufficient guidance in the specification and the breadth of the claims, it would

require an undue amount of experimentation for the skilled artisan to practice the invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 26-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paglia et al. (J. Exp. Med. 183: 317-322, January 1996) in view of Cohen et al (U.S. Patent 6,232,456, filed October 6, 1997).

The claims recite a method of producing immune-activated cells directed toward stratum corneum chymotrytic enzyme comprising the steps of exposing dendritic cells to a stratum corneum chymotrytic enzyme or any fragment thereof that lacks stratum corneum chymotrytic enzyme protease activity wherein said exposure to said stratum corneum chymotrytic enzyme or fragment thereof activates said dendritic cells thereby producing immune-activated cells directed toward stratum corneum chymotrytic enzyme, (2) the said method wherein said immune cells are B cells, T cells, and dendritic cells, (3) the said method wherein the dendritic cells are isolated from an individual prior to exposure to stratum corneum chymotrytic enzyme or any fragment

thereof wherein said dendritic cells are reintroduced into said individual subsequent to said exposure, (4) the said method wherein said individual with any cancer, or suspected of having any cancer or at risk of getting any cancer, and (5) the said method wherein the stratum corneum chymotrytic enzyme fragment "is" from 9 amino acids to 20 amino acids and the 9 amino acid fragment is selected from SEQ ID NOS 31, 32, 33, 34, 35, 36, 80, 86 and 99. For this rejection "is" recited in claim 28 is interpreted as "comprising", meaning that the stratum corneum chymotrytic enzyme fragment from 9 amino acids to 20 amino acid acids contains additional amino acid residues and thus, the claims encompass fragments comprising SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99 as well as the full-length stratum corneum chymotrytic enzyme comprising SEQ ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99.

Paglia et al teaches the priming of an immune response against a major histocompatibility complex class I-restricted antigen by utilizing dendritic cells (DC) for presentation of tumor-associated antigens (TAA), see summary. Paglia et al teaches that dendritic cells loaded in vitro with a model tumor antigen are able to prime cytotoxic T lymphocytes (CTLs) and provide an efficient in vivo immune reaction against tumors (see summary and pages 320-321). Paglia et al does not specifically teach a method of producing activated T cells directed toward the stratum corneum chymotrytic enzyme comprising the steps of exposing dendritic cells, which have been isolated from an individual prior to exposure to a stratum corneum chymotrytic enzyme comprising SEQ ID NOS:31, 32, 33, 34, 35, 36, 80, 86 and 99 and subsequent reintroduction of the dendritic cells. This deficiency is made up for in the teachings of Cohen et al.

Cohen et al teach the human serine protease, stratum corneum chymotrytic enzyme (see SEQ ID NO:33) comprising SEQ ID NOS:31, 32, 34, 80 and 99 (see the alignments attached to the back of this office action). This human serine protease is a target for the design and use of therapeutic treatments for prostate diseases, tumors or metastases (see column 7, lines 45-50).

It would have been prima facie obvious at the time of the claimed invention to produce a method of activating dendritic cells in vitro and re-administer the "activated" dendritic cells to prime CTLs against the stratum corneum chymotrytic enzyme comprising SEQ ID NOS: 31, 32, 34, 80 and 99 for therapeutic benefit in view of Paglia et al and Cohen et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have produced a method of activating dendritic cells in vitro and re-administer the "activated" dendritic cells to prime CTLs against the stratum corneum chymotrytic enzyme comprising SEQ ID NOS: 31, 32, 34, 80 and 99 for therapeutic benefit in view of Paglia et al and Cohen et al because Paglia et al teach that dendritic cells can be primed in vitro to present any tumor associated antigen (TAA) because they are particularly effective in stimulating both CD4 and CD8 naïve T lymphocytes", as well as "...generate T cell-mediated tumor-specific immunity..., see page 317 and Cohen et al teach the stratum corneum chymotrytic enzyme (see SEQ ID NO:33) comprising SEQ ID NOS:31, 32, 34, 80 and 99 as a target for the design and use of therapeutic treatments for prostate diseases, tumors or metastases and Cohen et al also teach that the disclosed serine proteases are known to be involved in proteolytic

processes, which are thought to be the critical point in tumor invasion and metastasis (see column 2, lines 43-52) Therefore, it would have been obvious to one skilled in the art to produce a stratum corneum chymotrytic enzyme that lacks protease activity for tumor therapy. Thus, it would have been obvious to one skilled in the art to have produced a method of activating dendritic cells in vitro and re-administer the "activated" dendritic cells to prime CTLs against the stratum corneum chymotrytic enzyme comprising SEQ ID NOS:31, 32, 34, 80 and 99 for therapeutic benefit in view of Paglia et al and Cohen et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 26-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-11 of

copending Application No. 10/372,521. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scope of the conflicting claims from both applications are drawn towards (1) a method of producing immune-activated cells directed towards stratum corneum chymotrytic enzyme comprising exposing immune cells to a stratum corneum chymotrytic enzyme or fragment thereof that lacks protease activity wherein the exposure activates said immune cells toward stratum corneum chymotrytic enzyme, (2) the said method wherein said immune cells are B cells, T cells, and dendritic cells, (3) the said method wherein the dendritic cells are isolated from an individual prior to exposure to stratum corneum chymotrytic enzyme or any fragment thereof wherein said dendritic cells are reintroduced into said individual subsequent to said exposure, (4) the said method wherein said individual with any cancer, or suspected of having any cancer or at risk of getting any cancer, and (5) the said method wherein any stratum corneum chymotrytic enzyme fragment "is" from 9 amino acids to 20 amino acids.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 26-31 directed to an invention not patentably distinct from claims 6-11 of commonly assigned Application No. 10/372,521. Specifically, see above.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned Application No. 10/372,21, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly

assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

Conclusion

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at (571) 272-0827 from 8:00 AM to 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571) 272-0871.

Official papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform to the notice published

in the Official Gazette, 1096 OG 30 (November 15, 1989). The official fax number for Group 1600 where this application or proceeding is assigned is (703) 872-9306.

Respectfully,
David J. Blanchard
571-272-0827

LARRY R. HELMS, PH.D
PRIMARY EXAMINER